ABSTRACT OF THE DISCLOSURE

Method of automated metabolic stability analysis of library of compounds by mass spectrometry using stable isotope labeled internal standards is provided. Said internal standards are prepared in situ by reaction of an authentic sample of said library compounds with a stable isotope labeled reagent. In an automated fashion, cytochrome P450 enzyme systems are added to said library compounds; said reactions are terminated after certain periods of time by addition of an organic solvent containing equal amounts of said labeled internal standards; said terminated enzyme reactions are treated with a non-labeled version of said stable isotope labeled reagent to convert remaining library compounds to compounds of identical structures, except the labeled atoms, as those of said labeled internal standards; said conversion reactions are extracted and the extracts are analyzed by isotope dilution mass spectrometry to determine the percentage of library compounds remaining after enzyme reactions.